THE KANSAS UNIVERSITY SCIENCE BULLETIN.

Vol. V, No. 4—October, 1909.
(Whole Series, Vol. XV, No. 4.)

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A Study of the Respiratory and Cardiac Activities and Blood Pressure in the Skate Following Intravenous Injections of Salt Solutions, ... *Ida H. Hyde.*

PUBLISHED BY THE UNIVERSITY,

LAWRENCE, KAN.

Entered at the post-office in Lawrence as second-class matter.

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A STUDY OF THE RESPIRATORY AND CARDIAC ACTIVITIES AND BLOOD PRESSURE IN THE SKATE FOLLOWING INTRAVENOUS INJECTIONS OF SALT SOLUTIONS.

BY IDA H. HYDE.

Plate X, and 49 figures.

(From the Marine Biological Laboratories of Woods Hole and Leland Stanford[1] and the Physiological Laboratory of the University of Kansas.)

THE experiments that are recorded in this article were conducted on the skate; *Raia erinacea* and *Raia binoculata*, during the summers of 1902, 1903, 1906 and 1907.

A host of articles have accumulated since Humboldt first studied the action of salt solutions upon the rhythmical changes in the heart's contractions; but with the progress of physical chemistry new problems and different views presented themselves and left many important questions still unsettled. To aid in solving some of these I undertook the study from a less general standpoint by employing a method and an animal seldom heretofore adopted in the solution of the questions. A few experiments were begun on the fresh-water sturgeon and on the frog in order to compare the results with those obtained with the skate. These, however, will be extended and varied before the results are published.

It was hoped that simultaneous records and comparisons of the three activities might throw some light upon the factors that influence them and indicate whether their nerve centers are alike stimulated by the same ions. At first the object was also to determine whether it was the anion or cathion that

1. I take this opportunity to express my hearty thanks to the directors for the privilege of working in these institutions and for the courtesies I received there.

stimulated the different centers, and if there were ions that simulated one but proved neutral or inhibitory to the other centers. Moreover, whether valency or solution tension were influential factors, and if the toxicity produced on either the respiratory, cardiac or vasomotor centers by certain salts could be counteracted by definite amounts of other salts that proved antitoxic. Before I had proceeded far, however, I desired, in addition to the solution of some of these questions, to study other physical and chemical effects that were produced in the body by the salts; *e. g.*, osmotic pressure, the products of chemical reactions, such as oxygen, carbon dioxide, hydrogen and hydroxyl ions, and the dosage of the solutions.

I realize that in experiments of this character a host of phenomena may exert their influence and that it is difficult with the data at hand to assign to any special one the cause that produces the particular result. Some of the events which may deserve consideration can, however, be controlled and their influence either accounted for or removed from further consideration. That is especially so in the investigation of the fishes, where the temperature and supply of the water can be controlled and are kept normal and constant throughout the experiment and where the amount of solution injected bears a direct proportion to the weight of the animal, and also where from the method employed mechanical stimulation, either due to the insertion of the cannula or brought about by retaining the fish in a definite position during the experiment, is avoided.

On the other hand, we assume that the addition of an isotonic salt solution to the blood, the chosen amount of which does not cause any change in any of the functions under consideration, will, if hypo- or hyper-tonic, produce various physical and chemical alterations both in the fluids and tissues of the body. Introducing an additional salt into the blood assumes changes in its osmotic pressure and in the contents of the corpuscles, also alterations in the permeability of the walls of the capillaries, corpuscles and other tissue cells. Or the new composition in blood salts may make new combinations with colloids or ferments or proferments, or set free ions that will thus stimulate or inhibit functions by acting directly on cardiac or muscle cells, or indirectly upon special centers. That is, the physiological property of the blood is altered by changing the proportion and character of the electrolytes in it, and this must have

its peculiar influence upon the life phenomena of respiration and heart action and blood pressure. To which of these must be ascribed the important changes produced in respiration and cardiac activity and blood pressure is a question with which I shall not for the present concern myself, since in addition to the experiments which I conducted it would be necessary, as I later saw, to carry on extensive physical and chemical investigations for which I lacked the time. I shall content myself, therefore, by simply stating my method and observations, and not attempt theoretical considerations of the underlying causes, trusting that the data obtained from over 200 experiments will aid in the correct interpretation of results secured by other investigators working upon problems related to those that I undertook.

According to Garry[2] and Sumner[3] the percentage of salts in the skate and selachian's blood does not differ from that in sea water. The lowering of the freezing point being —1.8° C. and the osmotic pressure twenty-two atmospheres, the sea water is therefore isotonic with the skate's blood, while Baglioni[3] estimated it isotonic with an m⅝ NaCl or a 2 per cent NaCl plus 2.5 per cent urea. Although the osmotic pressure of the selachian's blood is the same as sea water, its salt content is less, but the lowering of the freezing point is compensated by the urea in the blood.

Employing Welcker's method, I ascertained that a small skate weighing from 550 to 700 grams possessed 25 to 30 grams of blood, or about one-twentieth of the body weight. Harris[3] states that the weight of the blood in the skate is only one-fortieth of the body weight, but he does not describe the method employed for ascertaining his data.

Although there are wide variations in blood pressure, I found that the mean pressure for an average-sized skate was about 20 mm. of mercury.

The photograph on plate X illustrates one of the methods employed for securing records of the respiratory and cardiac action and blood pressure. The skate was placed ventral side up on an inclined board, partly submerged in water, and held in place by fish netting; a constant stream of fresh sea water

2. Garry, W. E. Biological Bulletin, 1905, vol. VIII, No. 4, p. 257.

3. Sumner, F. B. Bulletin Bureau of Fisheries, 1906, p. 596. Baglioni. Zentralblatt für Physiologie, 1905, vol. XIX, p. 12. Harris, D. F. Journal of Physiology, 1903, vol. XXX, Nos. 3 and 4, p. 319.

of a definite volume, velocity, and temperature entered the mouth through a forked glass tube covered with rubber tubing.

As soon as the water enters the mouth and flows out of the gill slits over the body, thus keeping the skate practically submerged, and the netting comes in contact with the body, the fish is perfectly quiet and remains so for hours, apparently contented and comfortable. A cannula, filled with 20 per cent glucose or glucose and 1 per cent ammonium oxalate, is inserted in one of the side branches of the aorta and joined to a delicate mercury manometer placed quite on a level with the blood vessels. To the open end of the manometer is attached a Hürthle manometer, which records the heart action, while the pressure is read off directly from the manometer.

By means of a silk loop one of the gill arches is attached to a light lever which records the respiratory movements. In control experiments the tip of the ventricle was exposed and by means of a silk loop joined to a light lever, so that in addition to the above records, separate ones were obtained of the rate and force of the heart's activity.

The salts employed in the experiments were all chemically pure, either from Kahlbaum or specially prepared in the laboratory, and they were all standardized. The water employed in making up the solutions was twice distilled in glass.

To avoid mechanical stimulation a cannula, to which was connected a rubber tube, was inserted either in the median or lateral caudal vein and tied in place. Subsequently 4 cc. of the solution per kilo weight of fish was slowly pressed from a graduated glass tube into the cannula by means of a rubber bulb attached to its upper end.

During the inspiratory phase the mouth and spiracles are opened, the floor of the mouth is lowered, the gill clefts or external branchial apertures are closed, and water enters the mouth and spiracles. In the expiratory phase the mouth and spiracles close, the floor of the mouth returns to its normal position or is elevated and the gill clefts open to allow the water to escape. Occasionally a peculiar spouting takes place during which water is thrown from the mouth and spiracles. This is observed in the aquarium also and may be due to irritation, touch, stimulation of the mucous lining of the mouth by slime particles or vitiated water.

I first investigated the effect of different concentrations of

the same solution, seeking the weakest solution that produced any change in the three functions under consideration; also, which concentration proved toxic, and whether the injurious dose could be modified or antagonized by a definite dose of another salt.

Observations were made and curves secured before, during and after the injection of the salt solutions. From one to five minutes after the injection a change in one or more of the functions under consideration usually occurred, and this was followed by a second change that lasted from five to twenty minutes, before the records again assumed their normal character. The first effect may be the reaction of the salt upon the constituents of the blood and indirectly upon muscle and nerve cells; the second is due to osmotic pressure changes. That injections of hypertonic salt solutions in the blood of the dog increases the osmotic pressure, which may become normal within twenty minutes, was proved by Magnus.[4] Moreover, those salts that set free O, CO_2, H, or OH ions, in their reactions, exert their influence more often through these ions, and effect results that differ from those produced by salts having the same cations, but do not react with the same resulting ion products; *e. g.*, NaCl is different in its effects from Na_2CO_3, probably because of the OH ions set free by the Na_2CO_3 dissociation.

It is possible that the blood pressure, respiratory and cardiac activities depend upon the number of molecules and ions in the blood, and upon the dissociation tension of the salts. The prepotent anions or cations may stimulate or inhibit enzyme action, and thus aid in producing the inner stimulus that affects alike the force of cardiac and respiratory activity and directly or indirectly the blood pressure.

A careful study of very many experiments with the same salts was made, the average results summed up, and the most typical of a series of experiments put in tabular form. Thus table II gives a survey of the different series of experiments and is a summary of all the experiments conducted on the skate with NaCl solutions. It shows that m/32, m/16, m/8, NaCl solutions produce as a rule practically no change in the heart or respiratory activity or blood pressure. An m5/8 NaCl solu-

4. Magnus. Archiv für Experimentelle Pathologie, 1900, vol. 44, p. 99.

tion (see curve 1) increases the force and blood pressure but leaves the rate of the heart and respiration unaltered.

An m/1 solution (curve 2) causes a rise in blood pressure and force of heart's rhythm at once, which usually continues for about twenty minutes. But the force and rate of respiration is either unchanged for one to two minutes and then decreases; or may, as does the heart rate, first decrease and then return to normal.

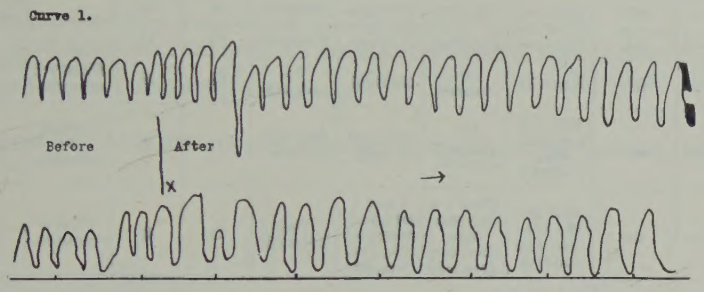
Following the injection of a 2m NaCl solution (curves 3 and 4) the blood pressure increased for about five minutes, then became normal. The rate and force of the heart and respiratory movements decreased for one to twenty-five minutes; but in many cases the force of the heart's activity first decreased for one to two minutes and then increased, or increased as the blood pressure rose. In every instance the systole and inspiratory phases were prolonged above normal with a 2m NaCl solution.

A *résumé* of the NaCl experiments shows that injections of 4 cc. per kilo fish of m/64 to m/8 solutions are as a rule practically indifferent; m⅝ stimulates the force of heart and respiratory activity and raises blood pressure for from one to five minutes, but is usually indifferent to rate; m/1 increases the force of the heart's action and also blood pressure, but the rate and force of respiratory activity differs in that they may for one minute remain normal, then decrease; or may, as does the heart rate, decrease for one to three minutes before resuming again the normal activity; 2m decreases rate and force of heart and respiration, but the heart's force is often increased after one to two minutes' decreased action. The blood pressure is raised during the first one to five minutes, then falls.

It might be concluded that the blood salts can be slightly increased by 4 cc. per kilo m/64 to m/8 without stimulating or inhibiting either of the three functions that are considered, and that equilibrium of the osmotic pressure is rapidly established. On the other hand, m⅝ stimulates the force of both heart and respiration. I infer that its effect is directly upon the nerve centers for one to five minutes, before the attraction of water to the blood establishes equilibrium. An increase to m/1 has a stimulating effect only upon the force of the cardiac center, thereby increasing also the blood pressure, but

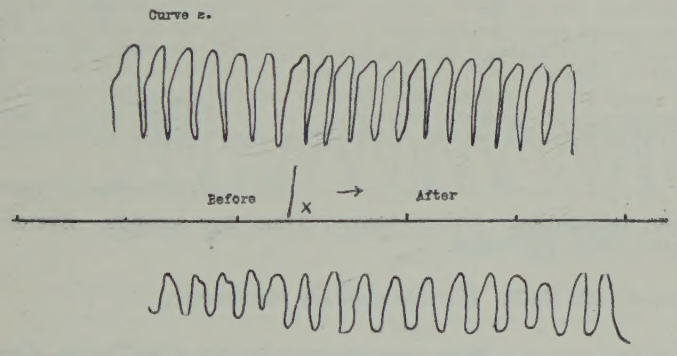
strangely enough does not affect the respiratory center in the same direction but rather depresses its force and rate, as well as the rate of the heart's activity. But a 2m solution has again a like depressing influence upon both force and rate of respiratory and cardiac rhythm and at first causes a rise in blood pressure.

CURVE 1. Following an injection of m⅝ NaCl. Lever attached to heart and gill arch.



Upper, respiration. Lower, cardiac curve. Injection at X. Force of heart and respiratory action increased, but not rate.

CURVE 2. After NaCl. Lever attached to heart and gill arch. Normal before X.



Upper, respiration. Lower, cardiac curve. Heart and respiratory rate unchanged; force of former increased but of latter unchanged or even less. Time, five seconds.

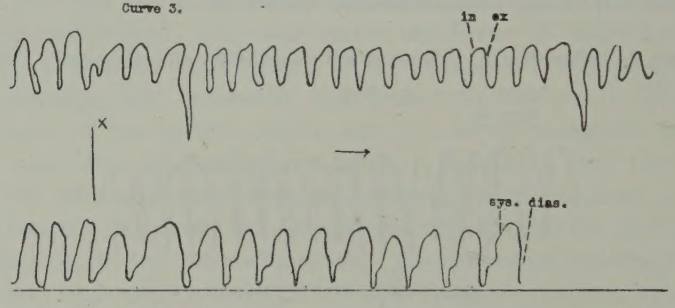
Data of the mean results in respiration, heart action and blood pressure of many experiments on the skate. Different

concentrations of NaCl were intravenously injected in the proportion of 4 cc. per kilo fish:

TABLE I. Effect of NaCl solutions.

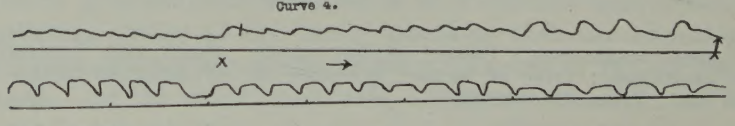
Salt amt.	Mol.	Heart rate.	Heart force.	Respiratory rate.	Respiratory force.	Blood pressure.		Time of change.	Curves.
						Normal.	Change		
NaCl 2 cc.	m/32	Neutral.	Neutral.	Neutral.	Neutral.	24	24		
NaCl 2 cc.	m/16	Neutral.	Neutral.	Neutral.	Neutral.	20	20		
NaCl 2 cc.	m/8	Neutral.	Neutral.	Neutral.	Neutral.	14	14		
NaCl 2 cc.	m⅝	Neutral.	Increased.	Neutral.	Increased.	26	28	First 1–5 minutes.	1
NaCl 2 cc.	m/1	Fell 1–3 minutes, then normal.	Increased at once.	Normal or less.	Normal or less.	17	20	During 20 minutes.	2
NaCl 2 cc.	2m	Fell 36–30; systole prolonged.	First 1–2 minutes rose, then decreased.	First 5 min. fell, inspiration prolonged.	Decreased.	20	23	First 5 minutes.	3, 4

CURVE 3. After 2m NaCl. Heart directly attached to lever.



Upper, respiration. Lower, heart. Time, five seconds. Systole and inspiration much prolonged.

CURVE 4. 2m NaCl. Hürthle mercury manometer.

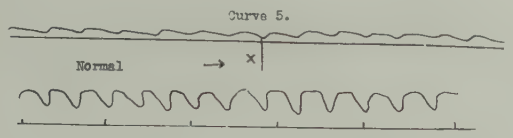


Normal, 10:35 A. M.
Heart rate, 36.
Respiration rate, 36.
Pressure, 20.

10:40 A. M.
Heart rate, force slightly increased.
Respiration rate 27, force slightly decreased.
Pressure, 23.

10:45 A. M.
Heart rate, 30, force increased.
Respiration rate 36, force less.
Pressure, 23.

CURVE 5. M/32 KCl. Heart and blood pressure were obtained with Hürthle manometer. For respiratory records the lever was attached to the gill arch.

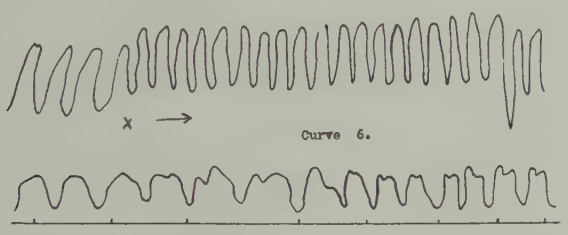


The upper curve heart, and from abscissa to heart blood-pressure record.

Below the latter respiratory curves, and the time in five seconds.

Blood pressure remained unchanged, respiratory rate decreased, force unaltered, expiratory phase prolonged. Heart rate from 24 to 22, prolonged diastole and force unchanged.

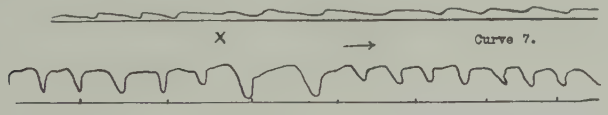
CURVE 6. M/8 KCl. Lever attached to the tip of the ventricle and gill arch.



Upper, respiratory curve. Lower, heart. Time in five seconds.

The first part of the upper curve of respiration, taken before injection, registered 36; immediately after, force slightly less, but the rate increased to 42, and in ten minutes was normal again. The first part of the lower heart curve before injecting was 34 per minute. For about twenty minutes it was less (27), with prolonged diastole, then gradually increasing during fifteen minutes to normal. Force was unchanged.

CURVE 7. Effect of m/8 KCl.

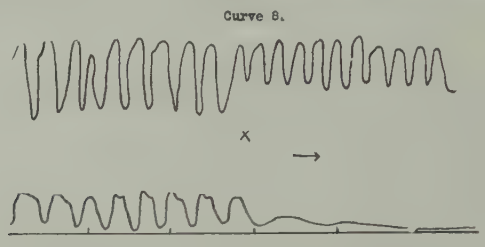


Upper, heart and pressure recorded with Hürthle mercury manometer.

Lower, respiratory records from lever attached to a gill arch.

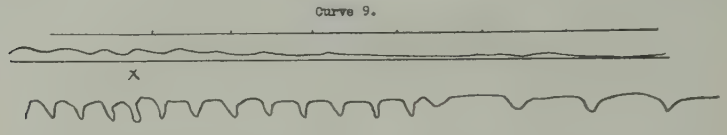
Pressure before injecting m/8 KCl 20 mm.; after injecting for two minutes 22 mm., then normal. After injecting the solution, the respiration for about twenty seconds decreased in rate with prolonged inspiration, then for about one minute increased, and in fifteen minutes was normal. Force was unchanged for twenty to sixty seconds, heart rate decreased with prolonged diastole, then in five minutes normal; force unchanged.

CURVE 8. M⅝ KCl. Curves secured with heart and respiratory levers.



Upper, respiration. Lower, heart curve.
Within one to two minutes after the m⅝ KCl was injected, the heart action ceased. Respiratory force decreased, rate increased, and stopped in twelve minutes.

CURVE 9. m⅝ KCl. Curves secured with lever and Hürthle manometer.



The upper are cardiac, the lower are respiratory records. Time, five seconds.
Within one minute blood pressure and heart action were zero. Respiratory rhythm decreased and in twenty minutes stopped.

TABLE II. Mean results in respiration, heart action and blood pressure following injection of different concentrations of KCl solutions.

Salt mol. 4 cc. per kilo.	Heart rate.	Time.	Heart force.	Respiratory rate.	Time.	Respiratory force.	Blood pressure.		Curves.
							Normal.	Change	
KCl m/100	Neutral.		Unchanged.	Unchanged.		Unchanged.	18	18	
KCl m/32	Slower.	20–60 sec.	Unchanged.	Increase, then less, or less at once.	20–60 sec.	Decreased or unchanged.	18 20	18 20	5
KCl m/8	Decreased.	20–60 sec.	Unchanged.	Decreased.	At once.	Unchanged.	20 20	18, 22, then 20	6 7
KCl m⅝	Decreased, then ceased.	5 sec.	Increased for 30 sec. then less.	Increased, stopped or decreased.	5 sec.; 7 min.	Decreased.	19 or 20	22, 1 min. 0. in 3 min.	8 9

The influence of KCl injections are summarized in table II, which represents the mean results of many experiments of the different series of KCl solutions. Curve 5 is a typical curve secured after injecting the usual amount of an m/32 KCl solution. From the table and the curve it is observed that an m/32

KCl solution produces a first effect of from twenty seconds to one minute upon the heart and respiratory activities. More often during this time the heart rate is slower, due to prolonged diastole, and the force remains unchanged. The inspiratory phase is, however, lessened while the expiratory is relatively prolonged.

Curves 6 and 7 represent records obtained with different methods after injecting an m/8 KCl solution. Although many other records were made these were chosen because they represent the more general type. There were exceptions in every case, but those variations were accounted for either because of the morbid condition of the skate, because it had been in the aquarium several days, or had been under observation for several hours and was fatigued or more or less irritable. After the solution was injected for from twenty to sixty seconds the heart activity greatly decreased and diastole was much prolonged. Occasionally the action increased above the normal rate for one to two minutes, and in ten to fifteen minutes was normal. The force remained unchanged. The respiratory rate as a rule decreased for fifteen to thirty seconds, with prolonged inspiratory phase, then either suddenly increased above normal or gradually returned to the normal rhythm. The force was usually unchanged. The blood pressure either fell or increased slightly, about 2 mm. mercury, for from one to two minutes.

Following the injection of m⅝ KCl, pressure fell either very suddenly to zero or in rapid leaps from 20 to 16 in one minute and zero in two minutes, or often 19 to 22 in one minute then zero within three minutes. The heart decreased in rate; *e. g.*, from 30 to 18, with increased force in one and zero in two minutes. Respiration slowed from 39 to 30 in five seconds to 18 and very shallow and often irregular and spasmodic in ten minutes, or rapid, 46 to 60, in five seconds, and gradually to zero in seven minutes, but in some cases continued active as long as twenty minutes after the heart had ceased contracting.

A *résumé* of the effects of KCl solutions brings to light that diastole and inspiratory phases are prolonged above normal in the different strengths of solution. Blood pressure falls in all but the most dilute solutions. The force of the heart and respiratory activity is practically unchanged in all but the toxic strength, m⅝, after which it decreases. The rate of the heart's

contractions as a rule is at first decreased in all strengths but the m/100; m⅝ is toxic to heart and respiratory activity, though usually the respiratory rhythm continues for five to twenty minutes after the heart has ceased.

A summary of some experiments that were undertaken to study what salts counteracted the toxic influence of KCl solutions is shown in table II*b*, and curves 10, 11, 12 and 13 illustrate a few of the experiments.

Curve 10 records the antitoxic effect of an m⅝ NaCl solution. The rate of the heart's action was 36, that of the respiratory 26. At 10:05 m⅝ KCl was injected; within a few seconds the heart action became irregular and respiration rapid, then irregular, with prolonged expiratory phases. Blood pressure fell. At 10:15, an injection of m⅝ NaCl was followed in a few seconds by regular and strong cardiac and respiratory contractions, which in ten minutes were quite normal, but the force of the heart-beat was stronger. In other experiments the toxic effect of an m⅜ KCl was quickly counteracted by an m/8 NaCl solution.

Curve 11 shows the favorable influence of $CaCl_2$ with or preceding a KCl solution; m/4 KCl following m/4 KCl+m/32 $CaCl_2$ shows a decrease in force of heart and respiratory activity, and a toxic m⅝ KCl following a mixture of m⅝ KCl+ m/32 $CaCl_2$ shows, in addition to a decrease in rate, a marked decrease in force, but in twenty minutes the heart and respiratory rhythm is almost normal. The $CaCl_2$ evidently proved antitoxic, and with KCl enhances the force of both respiratory and cardiac action.

Curve 12 also shows that a dose of m/4 $CaCl_2$ that preceded an m⅝ KCl and m/1 KCl counteracted their toxic effects.

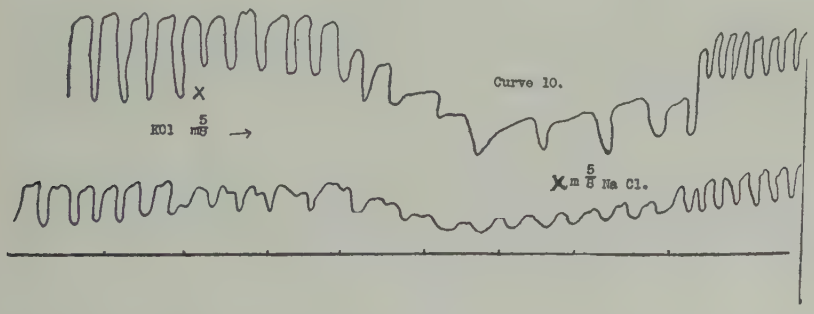
Curve 13: After $CaCl_2$ m⅛, blood pressure stood at 14 mm., heart action at 24, respiratory action at 36. When m⅝ KCl was injected, pressure fell to 2 mm, heart to four contractions and respiration increased to 42. At the end of two minutes pressure was again 14, heart and respiratory rate had increased, though shallow. At the end of five minutes, pressure and action of heart and respiration were quite normal, but respiratory rate more rapid. This shows that when stronger solutions of Ca are injected, and the blood is in excess of the normal, it counteracts the toxic effect of m⅝ solution of KCl quicker and the toxicity is less marked on respiratory than

heart action. In some experiments the toxic effect of KCl m5/8 was overcome if $CaCl_2$ was injected soon after the KCl solution.

TABLE IIb. Salts that counteracted the toxic effect of m5/8 KCl.

Salt amt.	Mol.	Heart.	Respiratory.	Blood pressure.	Antitoxic.	Mol.	Heart.	Respiratory.	Blood pressure.	Curves.
4 cc. KCl. per kilo.	m5/8	Irregular, then spasmodic.	Rapid, then spasmodic.	Pressure fell.	$NaCl_2$ cc. followed m5/8 KCl.	m5/8	Regular in two minutes.	Regular in two minutes.	Rose.	10
KCl	m/4 subsequent.	Rate unchanged, force less.	Rate increased, force less.		$CaCl_2$ + KCl. Preceded.	m/32 m/4	Rate unchanged, force increased.	Rate less, force increased.		11
KCl	m5/8 subsequent.	Rate and force less.	Rate and force less.		CaCl + KCl. Preceded.	m/32 m5/8	Rate and force increased.	Rate and force increased.		11
KCl	m5/8	Slight increase in rate and force	Rate slight increased, force less.		$CaCl_2$.	m/4	Stimulant force and rate antitoxic.	Stimulant force and rate antitoxic.	Rose.	12
KCl	m/1	Unchanged.			Preceded.					
KCl	m5/8 subsequent.	Almost stopped; in five minutes quite normal.	Rate increased, force fell, then normal.	Fell.	$CaCl_2$. Preceded. m5/8 KCl.	m1/8	24	36	Normal.	13

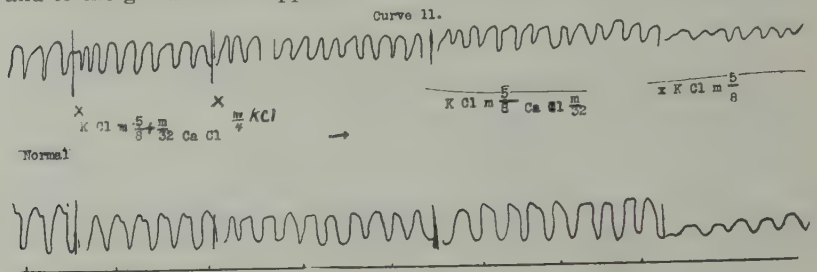
CURVE 10. Toxic action of KCl m5/8 counteracted by NaCl m5/8. Levers attached to ventricle and gill arch.



Time, five seconds. Upper, respiration. Lower, cardiac curves.[5]

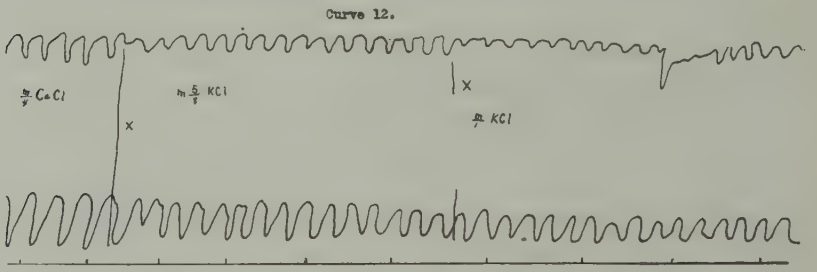
5. Within a few seconds after injecting m5/8 at X, the heart action became irregular and spasmodic in long diastole. In twenty-five seconds the greatly increased respiratory movements assumed prolonged expiratory spasms and a few seconds following m5/8 NaCl injection both respiratory and cardiac action became more regular again. m5/8 NaCl proved antitoxic for the toxic dose of m5/8 KCl.

CURVE 11. Toxic effect of KCl m⅝ counteracted by $CaCl_2$ m/32 for the upper curve. For lower curve, the lever was attached to the ventricle, and to the gill arch for upper.



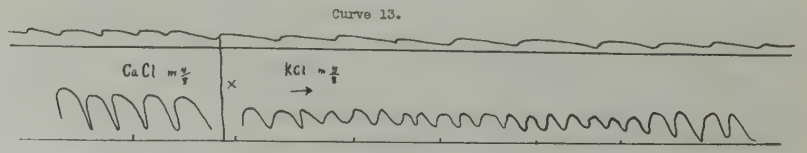
Showing the antitoxic and stimulating action of $CaCl_2$ 2 cc. m/4 KCl+ m/32 $CaCl_2$. Rate of heart contractions increased. KCl m/4 decreased the force of heart and respiration, while rate of respiration increased. The difference between the effect of m⅝ KCl and KCl m⅝ plus $CaCl_2$ m/32 demonstrates that $CaCl_2$ increases force of heart and respiration.

CURVE 12. Toxic effect of KCl m⅝ or m/1 counteracted by a previous dose of $CaCl_2$ m/4. For lower record the lever was attached to the ventricle, and to the gill arch for the upper curve.



Following 8 cc. of gradually increasing to m/4 doses of $CaCl_2$ the heart became distended and contracted more forcibly, due to the intracardiac pressure; m⅝ KCl injected increased the rate of cardiac and respiratory activity and an m/1 KCl injected ten minutes later failed to produce its usual toxic effect.

CURVE 13. KCl m⅝ following m⅛ $CaCl_2$. After m⅛ $CaCl_2$ was injected the pressure stood 14 mm., heart rate 24 and respiratory 36. At 3:50 P. M. KCl m⅝ was injected. In one minute pressure fell to 2 mm., heart rate to 4 and respiratory rate increased to 42. At the end of two minutes pressure stood 14, heart force increased rate 8, respiratory rate 48, force less. At the end of five minutes pressure and heart action were quite normal while respiration was abnormal in rate but normal in force.



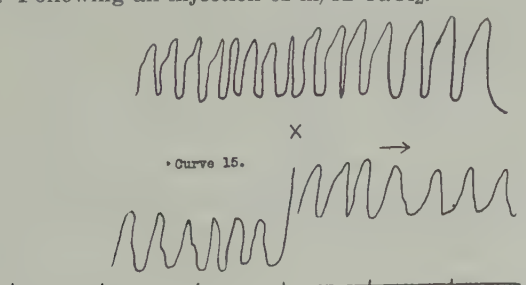
Upper curve, heart and pressure from abscissa. Lower curves, respiration. Time, five seconds. Records with Hürthle and lever manometer.

The results of the experiments with $CaCl_2$ are briefly tabulated in table III and partly shown in curves. It was observed that after an injection of the usual amount of m/32 $CaCl_2$ solution (curves 15, 16), the blood pressure remained unchanged. Respiratory activity was usually increased for one to three minutes, and the cardiac contractions continued unchanged or did so after about one minute of decreased rate and increased force. Following an injection of an m/8 $CaCl_2$ solution, the rate of cardiac and respiratory activity is usually decreased and the force of both increased. The blood pressure rises for about one minute. Often systole and inspiratory phases predominate, and furthermore, the solution proved antitoxic to many toxic salt solutions. The effect of an m5/8 $CaCl_2$ was first a decrease in rate of cardiac and respiratory activity, often irregular, with prolonged systole and inspiratory phases. The force of both activities was usually increased, as was also the blood pressure, for from one to three minutes. If the force of the heart-beat was not increased the blood pressure did not rise above normal.

TABLE III. Mean results in respiration, heart action and blood pressure, following injections of different concentrations of $CaCl_2$ solutions.

Salt mol.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.		Curves.
							Normal.	Change	
$CaCl_2$ m/32	Unchanged or decreased.	Unchanged or increased.	1 min.	Unchanged or increased.	Unchanged or increased.	3 min.	20	20	15, 16
$CaCl_2$ m/8	Decreased or unchanged.	Increased or unchanged.	1-3 min.	Unchanged or decreased.	Unchanged or increased.	1-3 min.	17	18	17, 18
$CaCl_2$ m5/8	Decreased or irregular.	Increased.	1-3 min.	Decreased or irregular.	Increased.	1-3 min.	22	24, 22	19, 20

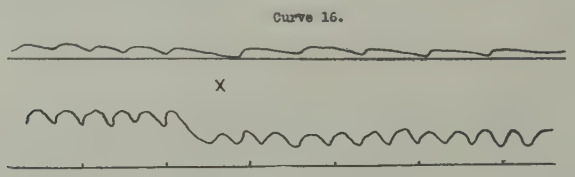
CURVE 15. Following an injection of m/32 $CaCl_2$.



Rate less and force of heart unchanged; rate of respiratory activity decreased for one minute, then normal, force increased.

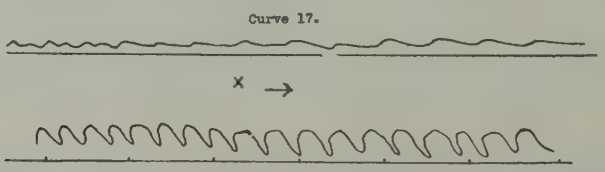
The upper respiratory and the lower cardiac records were secured with levers directly attached to gill arch and apex of heart.

CURVE 16. After m/32 $CaCl_2$.



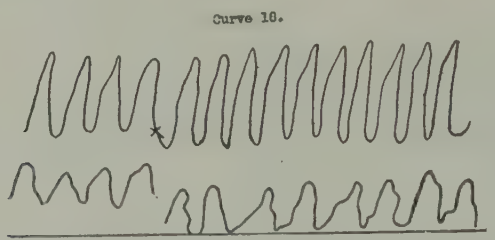
The upper curve, Hürthle manometer heart record. Lower curve, gill-arch lever records of respiratory activity. Rate of heart decreased, force unchanged. Respiratory activity and pressure unchanged.

CURVE 17. Effect of m/8 $CaCl_2$.



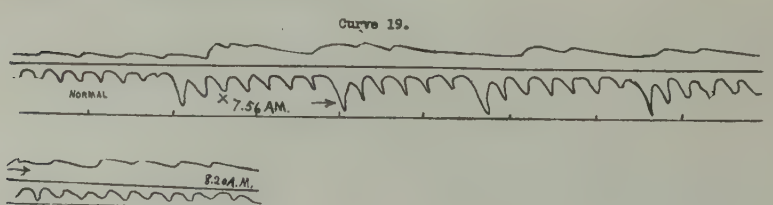
The upper curve is a record of the cardiac and blood-pressure changes secured with a Hürthle manometer. The lower respiratory is a gill-arch lever record. Rate decreased, force increased for both activities and blood pressure showed slight rise for a minute or two.

CURVE 18. Effect of m/8 $CaCl_2$.



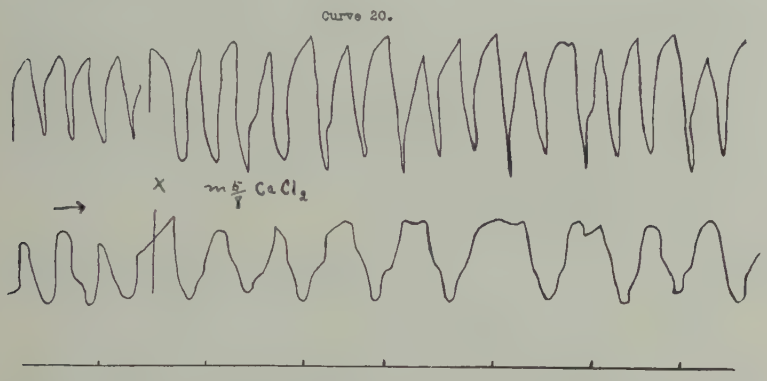
Upper, cardiac record secured with lever attached to the heart. Lower, gill-arch record. Respiratory rate unchanged, force increased. Cardiac rate decreased, force increased.

CURVE 19. Effect of m⅝ $CaCl_2$.



Hürthle cardiac records above, gill-arch lever records below. Time, five seconds. Cardiac and respiratory rate decreased, force and blood pressure increased for about three minutes, then quite normal for about thirty minutes. First effect often irregular and spasmodic, especially for cardiac rhythm.

CURVE 20. Effect of m⅝ $CaCl_2$.



Upper curve respiratory, lower cardiac. Levers directly attached to heart and gill arch. Cardiac and respiratory rates first decreased, force increased; irregular prolonged diastole and inspiratory phases.

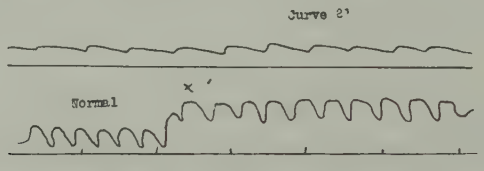
The results following injections of $MgSO_4$ solutions are summarized in table IV, and illustrated in the curves. It was observed that an m/64 or m/8 $MgSO_4$ had a more depressing influence on respiration than on cardiac activity. The rate was either unchanged or less, but force and blood pressure usually slightly greater for cardiac, while rate and force of respiratory activity were generally decreased.

An m⅝ or m/1 solution produces for about two minutes an increase in blood pressure followed by a decrease. Respiratory and cardiac rate and force both decrease, but occasionally the force of the heart's activity is first increased. Sensory reflexes are all reduced. With every strength of the solution the force and rate of the respiratory rhythm and the cardiac rate were decreased, but blood pressure and cardiac force were increased or decreased after a previous increase. With strong solutions, *e. g.*, m/1, diastole and expiratory phases predominated and the activities may become irregular, but an m/8 $CaCl_2$ overcomes the toxic effect and increases the force of the respiratory phase and blood pressure.

TABLE IV. Mean results in cardiac and respiratory activity and blood pressure following injection of different concentrations of $MgSO_4$.

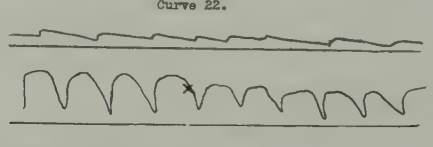
Salt mol.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Pressure change.	Curves.
$MgSO_4$ m/64	Less or unchanged.	Unchanged or increased.	15 min.	Less or unchanged.	Less.	15 min.	20	21 20	21
$MgSO_4$ m/8	Less or unchanged.	Increased or unchanged.	5 min.	Less or unchanged.	Less.	5 min.	18	19 18	22
m5/8 or m/1	Less or unchanged.	Decreased after rise.	Rise 2 m.	Less.	Less.	3 min.	22	23 21	23

CURVE 21. Effect of $MgSO_4$ m/64.



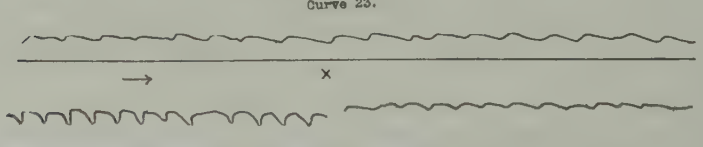
Upper curves, cardiac and pressure with Hürthle. Lower, respiratory gill-arch lever. Time, five seconds. At x, injection. Cardiac rate less, force and blood pressure slightly greater; respiratory rate less, force unchanged.

CURVE 22. Effect of $MgSO_4$ m/8.



Upper curve, cardiac and blood pressure shows decrease in cardiac rate, slight increase in force and blood pressure, for two minutes. Lower, respiratory gill-arch lever curve; decrease in force, not in rate.

CURVE 23. Effect of $MgSO_4$ m5/8.



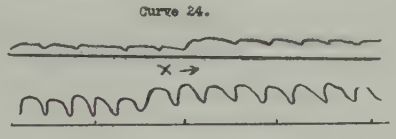
Upper curves, cardiac and blood pressure; rate unchanged, force and blood pressure slightly increase for two minutes, then decrease. Lower, respiratory curve, decrease in rate and force.

The effects of Na_2CO_3 injections are tabulated in table V. It was observed that Na_2CO_3 solutions are most effective in strengthening the force of the cardiac rhythm and thus raising the blood pressure. They do not stimulate respiratory activity except in strong doses, when they may increase the force. Its pronounced influence upon the heart may be due to OH ions that are set free by the dissociation.

TABLE V. *Résumé* of Na_2CO_3 injections upon cardiac and respiratory activity and blood pressure.

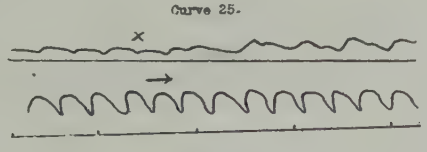
Salt.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Pressure changes.	Curves.
Na_2CO_3 m/32	Unchanged.	Increased.	15 min.	Unchanged.	Unchanged.		22	24	24
m/8	Unchanged or less.	Increased.	15 min.	Unchanged.	Unchanged.		20	23	25
m%	Unchanged or less.	Increased.	2 min.	Unchanged or decreased.	Increased.		26	28	26

CURVE 24. Effect of Na_2CO_3 m/32.



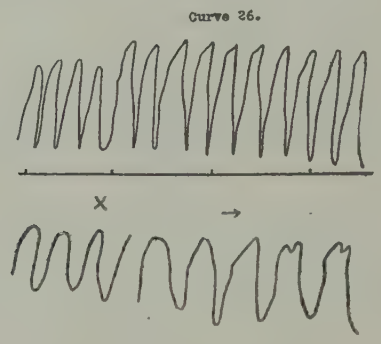
Upper curves, cardiac and blood pressure with Hürthle. Rate unchanged, force and blood pressure increased. Lower, respiratory; force and rate unchanged. Time, five seconds.

CURVE 25. Na_2CO_3 m/8.



Upper curves, cardiac and blood pressure. Rate decreased, force greatly increased, pressure rose. Lower curve, respiratory; force and rate unchanged. Time, five seconds.

CURVE 26. Na_2CO_3 m/2.



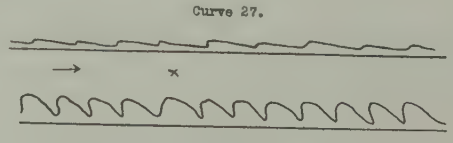
Upper, respiratory gill-arch lever records. Increased force, decreased rate. Lower, cardiac lever directly attached to heart. Increased force, decreased rate. Time, five seconds.

Na_2HPO_4 solutions are not so stimulating to cardiac rhythm as are Na_2CO_3 solutions. This is shown in table VI. Moreover, for the same strength they are more toxic. The solutions act like Na_2CO_3 chiefly upon the force of the cardiac action and are indifferent in weak solutions on respiratory movements.

TABLE VI. A summary of experiments of intravenous injections of Na_2HPO_4 relating to cardiac and respiratory activity and blood pressure.

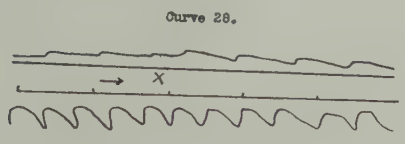
Mol. sol.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Change.	Curves.
Na_2HPO_4 m/64	Less or unchanged.	Increased or unchanged.	5 min.	Unchanged.	Decreased.	5 min.	23	24	27
m/8	Less or unchanged.	Increased or unchanged.	5 min.	Increased or unchanged.	Decreased.	5 min.	24	22	28
m/4	Less, then rapid or stopped.	Less.	5 min.	Less, then rapid.	Decreased.	3 min.	23	18	29

CURVE 27. Effect of Na_2HPO_4 m/64.



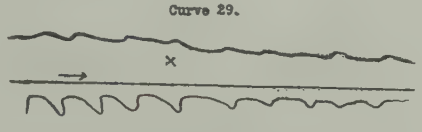
Upper, cardiac and blood-pressure Hürthle manometer curves; show force of heart action and blood pressure; slight increase, rate decrease. Lower, respiratory rhythm unaltered. Time, 5 seconds.

CURVE 28. Effect of Na_2HPO_4 m/8.



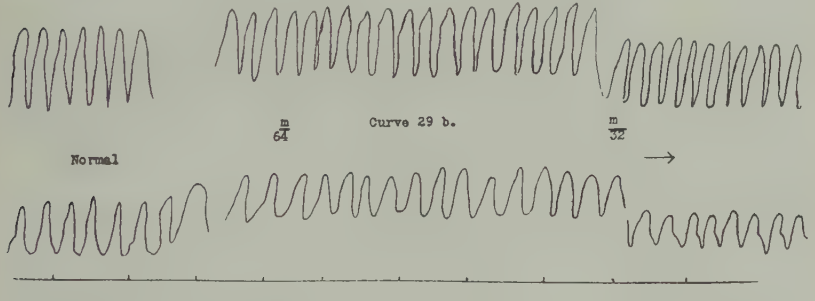
Upper, cardiac and blood-pressure Hürthle manometer curves. Rate little less, force slight increase. Lower, respiratory record; shows rate unchanged, force decreased, pressure decreased.

CURVE 29. Na_2HPO_4 m/4.



Upper, cardiac and blood-pressure Hürthle curves; show fall in blood pressure and for three minutes almost cessation of cardiac action. Lower, respiratory, force much decreased.

CURVE 29*b*. Effect of gradually increasing strength of Na_2HPO_4 solutions.



Upper, respiratory gill-arch lever curves show that with increasing strengths from m/64, m/32, m/8, m/4, solutions that the rate increased and force decreased from the normal and that this solution is more favorable to respiration as stimulating rate. Lower, cardiac apex lever curve shows that the rate remained practically unchanged except in m/4, when it became rapid and force decreased gradually from the normal.

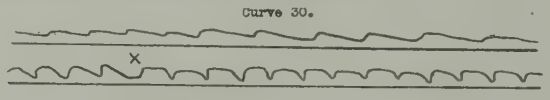
The influence of NaOH solutions is briefly tabulated in table VII. It is demonstrated that it acts, augmenting in all concentrations, on the force of the heart-beat and has not the same but rather a depressing effect on the respiratory center. The OH ions here, as in the Na_2CO_3, are the stimulating factors, but act more powerfully than in Na_2CO_3 solutions. The

respiratory force decreases with increased strength of the solution, while the blood pressure rises in all concentrations employed, showing that increase in blood pressure is not necessarily associated with rise of respiratory activity but rather with force of heart-beat.

TABLE VII Showing the effect of NaOH solutions upon respiratory, cardiac and blood-pressure changes.

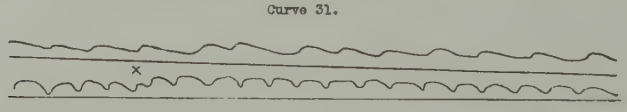
Salt mol.	Heart rate	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Pressure.	Pressure change	Curves.
NaOH m/64	Unchanged or less.	Increased.	5 min.	Unchanged.	Unchanged.	25	26	30
m/32	Unchanged or less.	Much increased.	15 min.	Decreased or unchanged.	Decreased or unchanged.	24	29	31
m/8	Unchanged.	Increased.	10 min.	Increased.	Decreased.	24	27	32
m/4	Less or unchanged.	Increased.	10 min.	Unchanged or increased.	Decreased.	26	29	33

CURVE 30. Effect of m/64 NaOH injections.



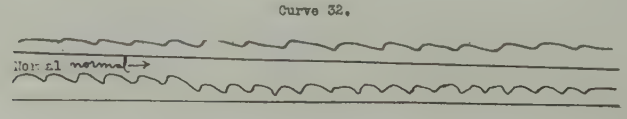
Upper, Hürthle curves of cardiac and blood-pressure changes; decrease in rate, increase in force and blood pressure for two minutes. Lower, gill-arch lever curves of respiratory changes unaltered.

CURVE 31. Effect of m/32 NaOH solutions.



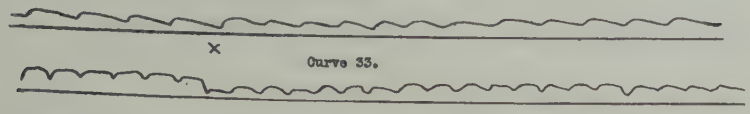
Upper, Hürthle curves of cardiac and blood-pressure changes show a first effect of two minutes of greatly increased force and slight decrease in rate of cardiac rhythm. The blood pressure increased for two minutes, respiratory rhythm decreased very little if at all.

CURVE 32. Effect of m/8 NaOH solutions.



Upper, Hürthle curves of cardiac and blood-pressure changes show increased blood pressure and rhythm. Lower, respiratory curves, increased rate but decreased force.

CURVE 33. Effect of m/4 NaOH solutions.



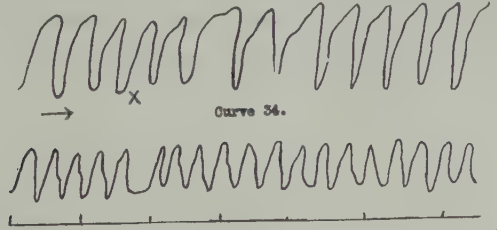
Upper curves, blood pressure and force of cardiac rhythm increased. Lower, respiratory activity decreased in force, rate increased.

From the series of experiments with different concentrations of urea solutions the conclusion is drawn that injection of urea solutions of high concentrations, 2m to 4m, increases force of respiratory and cardiac activity mainly. The rate is practically unchanged, and weaker solutions are quite indifferent on blood pressure, cardiac and respiratory activity. It has been found by Schröder[6] that selachian's blood normally contains 2.6 per cent of urea, and Baglioni[7] found that the selachian's heart beats longer in urea than in NaCl. According to Loeb it is due to the OH ions which are present when the dissociation of the urea occurs. A weak solution of m/20 of Na_2CO_3, to which a 2m urea solution has been added, greatly increased the force of cardiac action and blood pressure.

TABLE VIII. Effect of urea solutions.

Salt mol.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Pressure changes.	Curves.
Urea, m/50	Unchanged.	Unchanged.	15 min.	Unaltered.	Unchanged.	15 min.	20	20	
m/1	Unaltered.	Unaltered.	15 min.	Unaltered or less.	Unaltered or increase.	1 min.	21	21	34
2m.	Slight rise.	Slight increase.	2 min.	Unchanged.	Unaltered.	15 min.	20	20	35
4m.	Unchanged.	Increase.		Unchanged.	Increase.		22	21	36

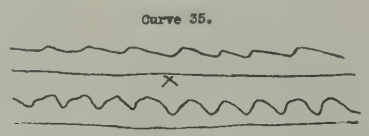
CURVE 34. Urea m/1.



6. Schröder. V. Zeitschrift für Physiologische Chemie, XIV, S. 596.
7. Baglioni. Zentralblatt für Physiologie, 1905, XXX, No. 12.

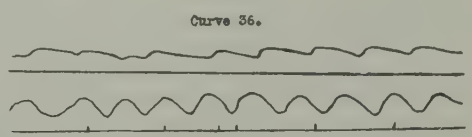
Upper, respiratory curve, with lever attached to gill arch, shows first decrease in rate for about one minute, then rate normal, force slightly increased. Lower, cardiac curve, with lever attached to apex. Cardiac activity unaltered.

CURVE 35. Urea 2m.



Upper, Hürthle cardiac record shows little increase in force and rate. Lower, respiratory rate and force unaltered.

CURVE 36. Urea 4m.



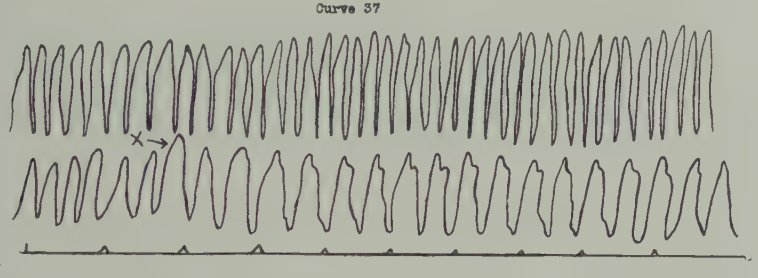
Upper, Hürthle cardiac curve; increased in force and pressure, rate unchanged. Lower, respiratory curve; force slight rise, rate unchanged.

The results obtained with standardized HCl solutions are tabulated in table IX. The weaker solutions, ranging from m/100 to m/64, increase for the first minute or two the force of the cardiac and respiratory and blood-pressure changes, and decrease or act indifferently on the rate of respiratory and cardiac activity. A stronger solution, m/32, for the first minute or two decreases the rate but usually increases the force of both the respiratory and heart action, and the blood pressure usually rises for the first minute; m/8 is toxic, but the respiratory rhythm continues several minutes after the heart ceases, or if it continues it is rapid and faint and the respiratory movements are continued with less force and rate. It is supposed that the stimulating action is due to the H ions. In all concentrations between m/100 and m/16 there is an initial increase in pressure and force, followed by a decrease in all activities before a return to either normal or less.

TABLE IX. Effect of HCl solutions.

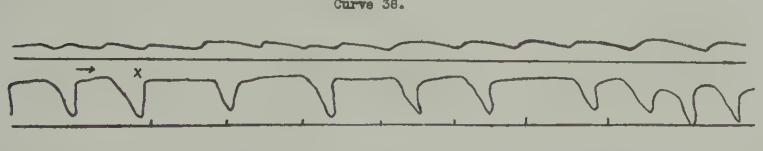
Salt mol.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Pressure changes.	Curves.
HCl m/64	Decreased.	Increased.	2 min.	Unchanged.	Increased or unchanged.	2 min.	19	20	37
m/32	Decreased.	Increased.	1 min.	Decreased.	Unchanged or increased.	1 min.	24	26	38
m/8	Rapid.	Weak.	1 min., then decreased.	Increased.	Unchanged or increased.	1 min., then decreased	21	10 0	39

CURVE 37. Effect of m/64 HCl on cardiac and respiratory activity and blood pressure.



Upper, gill-arch lever respiratory curve shows for two minutes increased force, rate unchanged. Lower, apex lever cardiac curve for two minutes increased force, decreased rate.

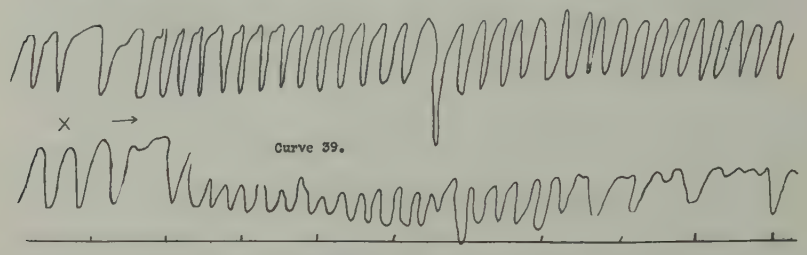
CURVE 38. m/32 HCl injection.



Upper, cardiac Hürthle manometer curve and blood pressure shows decreased rate and increased force and rise of blood pressure for one minute.

Lower, gill-arch lever record of respiratory activity shows rate less, force unchanged for one minute.

CURVE 39. Effect of m/8 HCl on cardiac, respiratory and blood pressure changes.



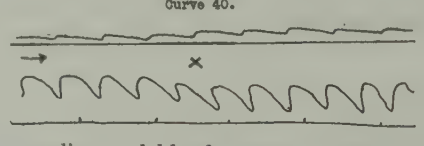
Upper, gill-arch lever respiratory curve shows increase at first of rate and force, then gradual decrease. Lower, apex lever curve shows at once fall in force and rapid heart-beat that soon becomes irregular and spasmodic before ceasing.

Injection of different strengths of NH_4Cl solutions show that weak solutions are quite indifferent. An m/8 solution increases blood pressure and force of respiratory movements, but an m$\frac{5}{8}$ depresses cardiac and blood pressure activities and greatly stimulates the expiratory phase of respiration, causing an irregular spasmodic rhythm for fifteen minutes, and this is replaced by a weak but regular activity.

TABLE X. Effect of NH_4Cl solutions.

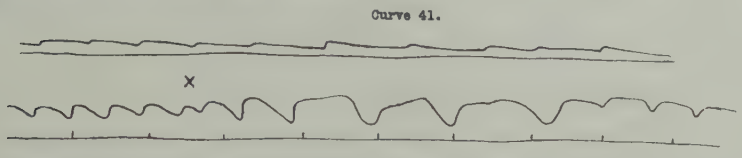
Salt. mol.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Pressure changes.	Curves.
NH_4Cl m/64	Unchanged or less.	Unchanged.	3 min.	Unchanged or increased.	Unchanged or less.	5 min.	26	26	
m/8	Unchanged or less.	Unchanged.	45 min.	Unchanged.	Expiration increased.	15 min.	26	28	40
m$\frac{5}{8}$	Much less.	Much less.	15	Long expiratory, irregular.	First increase, then regular or less.	15	26	22	41

CURVE 40. Influence of NH_4Cl m/8 on cardiac respiratory and blood-pressure changes.



Upper, Hürthle cardiac and blood-pressure curves show that rate and force are unchanged, blood pressure rose. Lower, respiratory curve; rate unchanged, force slight increase.

CURVE 41. Effect of m⅝ NH_4Cl.



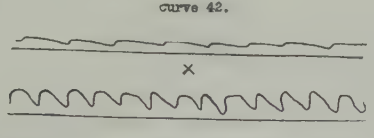
Upper, Hürthle cardiac and blood pressure show a decrease in cardiac activity and blood pressure. Lower, respiratory curve; for fifteen minutes prolonged expiratory phase and irregular rhythm, then weak but regular.

Effects of dehydrated chemically pure Na_2SO_4 solutions are most pronounced in the strong concentration of m/2 and m/1, both of which increase the force of cardiac, respiratory and blood-pressure activities, leaving the rate unchanged. The effect lasts longer with the weaker solution, and the after-effects are not, as with the saturated m/1 solution, a weakening of the rhythm and fall in pressure.

TABLE XI. Summary of Na_2SO_4 effects on respiratory cardiac, and blood-pressure changes.

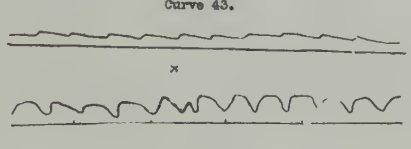
Salt mol.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Pressure change	Curves.
Na_2SO_4 m/64	Unchanged.	Unchanged.	15 min.	Unchanged.	Unchanged.	15 min.	26	26	42
m/2	Unchanged.	Slight increase.	15 min.	Unchanged.	Slight increase.	15 min.	26	27	43
m/1	Unchanged.	Slight increase.	5 min.	Unchanged.	Increased.	5 min.	27	29	44

CURVE 42. Effect of m/64 Na_2SO_4.



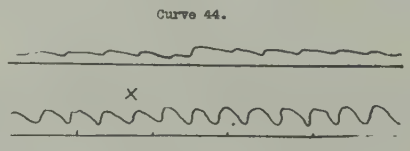
Upper, Hürthle cardiac and blood-pressure curve, and lower, respiratory, all show no change after injection of the solution.

CURVE 43. Effect of m/2 Na_2SO_4.



Upper, Hürthle cardiac and blood-pressure curves; rate unchanged, force and pressure slight increase. Lower, respiratory curve; rate unchanged, force increased.

CURVE 44. Effect of m/1 Na_2SO_4.



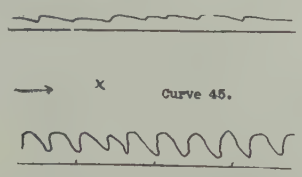
Upper, cardiac and blood-pressure curves, show slight increase in force and pressure, rate unchanged. Lower, respiratory; rate unchanged, force increased.

The effects of intravenous injections of $BaCl_2$ solutions are increased irritability and increased force and blood pressure, especially with weak solutions. Like most of the other salt solutions, it does not increase the rate of either heart or respiratory activity. In strong solutions it is toxic, producing at first irregular spasmodic cardiac and respiratory phases with strong diastolic and expiratory phases and with rise of blood pressure, or cessation of activity. The toxic effects can be avoided if small doses are injected with gradually increasing strengths, and the toxic effect is overcome by injections of $CaCl_2$ solutions.

TABLE XII. Effect of $BaCl_2$ on cardiac, respiratory and blood-pressure changes.

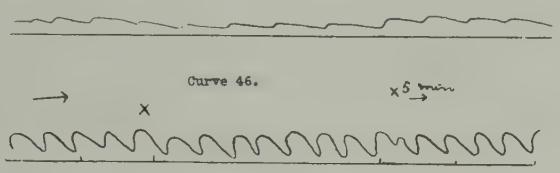
Salt mol.	Heart rate.	Heart force.	dura-tion.	Respir-atory rate.	Respir-atory force.	Dura-tion.	Pres-sure.	Pres-sure change	Curves.
$BaCl_2$ m/64	Un-changed.	In-creased diastole.	15 min.	Un-changed or slightly less.	Expira-tion in-creased.	2 min.	18 mm.	20 mm.	45
m/32	Un-changed.	Un-changed or in-creased.	1 min. 8 min.	Un-changed.	In-creased.	After 8 min.	16	16 18 14	46
m/8	Un-changed or slow or spas-modic.	In-creased irrita-bility.	2–5 min.	Stops or rapid spas-modic.		10–20 min. 2 min.	23	25	47
m/4	Toxic.			Toxic.					

CURVE 45. Effect of m/64 $BaCl_2$.



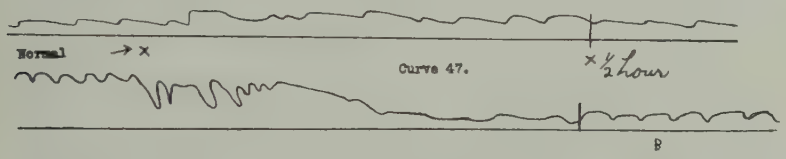
Upper, cardiac curve; rate unchanged, force and blood pressure slight increase. Lower, respiratory curve; rate unchanged, force increased.

CURVE 46. Effect of m/32 $BaCl_2$.



Upper, Hürthle cardiac curves; after one minute, rate, force and pressure unchanged. In five minutes, force and pressure increased. Lower, respiratory curve, shows rate unchanged, force increased.

CURVE 47. Effect of m/8 $BaCl_2$.



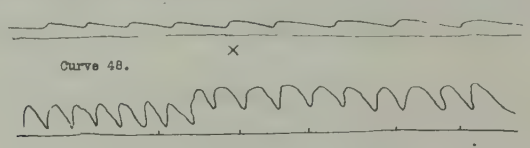
B half an hour after A. Upper curves of A and B, cardiac and blood-pressure records, show first spasmodic activity, then strong force and increased pressure. These activities decrease in half an hour but the rate continues unchanged. Lower, respiratory curve, shows first spasmodic action, then this stops for twenty minutes. In half an hour it is weak and slower.

The effect of distilled water passes off quite rapidly. For the first two minutes the rate of cardiac and respiratory activity is lessened and the force of the heart-beat and blood pressure slightly increased. The blood is rapidly affected and clots easily; soon the equilibrium of salts is again established and the normal action resumed.

TABLE XIII. Showing the effect of distilled water.

Distilled H_2O.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Pressure changes.	Curves.
3-4 cc.	Decrease.	Slight increase.	2 min.	Decreased.	Unchanged.	2 min.	24	26 24	48

CURVE 48. Effect of distilled water.



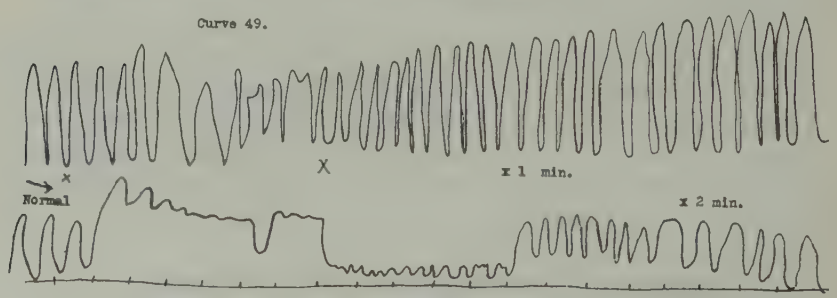
Upper, Hürthle cardiac and blood-pressure curves, show decrease in rate, slight rise in force and blood pressure for two minutes, then normal. Lower, respiratory lever, gill-arch curve, shows decrease in rate, force unchanged for two minutes.

Acid sodium phosphate solutions cause an increase in force of respiratory and cardiac activity, and for the weaker solutions at first also an increase in rate. Diastolic and inspiratory phases are often prolonged and the toxic effect is overcome by an alkali solution of sodium phosphate or one of $CaCl_2$.

TABLE XIV. Showing mean results of NaH_2PO_4 solutions.

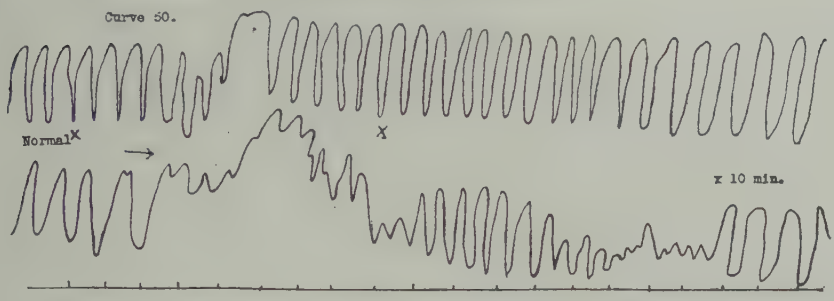
Mol. solution.	Heart rate.	Heart force.	Duration.	Respiratory rate.	Respiratory force.	Duration.	Pressure.	Pressure change	Curves.
m/64	Rapid to normal in two minutes.	Weak, increase.	1 min. 2 min.	Increased. Normal.	Less increase.	1 min. 2 min.			49
m/16	Increase.	Increase. Decrease. Normal.	1 min. 2d min. 10 min.	Unchanged.	Increased.	10 min.			50
m/8	Decreased. Normal.	Increased. Normal.	1 min. 5 min.	Increased.	Increased.	10 min.			51

CURVE 49. Effect of m/64 NaH_2PO_4 solutions.



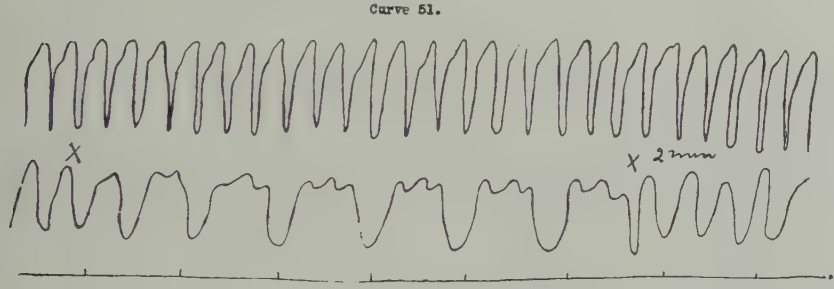
Upper records of respiratory activity before, during and following for two minutes the injection of an m/64 acid phosphate solution. First minute rate greatly increased, force less; within two minutes force gradually increased to slightly above normal and rate normal. The lower cardiac record shows first rapid contractions that increase during the second minute in force, becoming normal in rate and force in two minutes.

CURVE 50. Effect of m/16 NaH_2PO_4 solutions.



Upper, gill-arch lever records of respiratory activity, show increase in force, rate unchanged. Lower, cardiac lever, records first an increase in rate and force; second, rapid, shallow; in ten minutes quite normal in rate and force.

CURVE 51. m/8 NaH_2Po_4 solutions.



Upper, gill-arch lever records of respiration show increase in rate, and after two minutes also in force; inspiration prolonged. Lower, cardiac apex records. First minute prolonged diastole and increased force, followed by slower rate; in five minutes quite normal in rate and force.

TABLE XV. A general survey of the stimulating and depressing effects.

Stimulating, salt mol.	Heart force.	Heart rate.	Respiratory rate.	Respiratory force.	Blood pressure.	Duration.	Depressing salt mol.	Heart rate.	Heart force.	Respiratory rate.	Respiratory force.	Blood pressure.	Remarks.
NaCl m/1 m⅝	Increased.	Unchanged.	Unaltered.	Increased.	Rose.	m⅝ 5 min. m/1 15 min.	NaCl m/1	Less.		Less.	Unchanged.		
NaCl m 2	Rise.	Systole long.		Inspiration long.	Rose.	2 min.	NaCl m 2	Less.	After 2 min. less.	Less.	Less.	Fall after 2 min.	Weak sol. stimulates, Strong depressess.
KCl m/32 m/8			m/8 Rose.				KCl m/32 m/8	Less.	Unchanged.	Less.	Unchanged or less.	Unchanged or less.	m⅝ toxic. Depresses,
$CaCl_2$ m 32 m⅝	Rose.			Rose.	Rose.	1-3 min.	$CaCl_2$ m/32 ⅝	Unchanged or less.		Unchanged or less.			m⅝ depresses. Often toxic.
$MgSO_4$ m 24 m/1					Rose.	1-15 min.	$MgSO_4$ m/64 m/1	Less.		Less.	Less.		Depressing.
Na_2CO_3 m 32 m⅝	Rose.			m⅝ Rose.	Rose.	1-15 min.	Na_2CO_3 m 32 ⅝	Less.		Unchanged.	Unchanged.		Strong cardiac stim. and raises blood pres.
Na_2HPO m/64 m/4	m/8 Rise.						Na_2HPO_4 m/64 m/4		m/4 less.	Unchanged.	Less.	Fall.	Weak sol. stimulates, strong depresses heart force.
NaOH m/64 m/4	Rise.		m/8+m/4 Rise.		Rise.	5-15 min.	NaOH m/64 m/4	m/64 m/32 Less.			Less.		Strong sol. decreases force of respir.
Urea m/1 4m	Rise.			Rise.			Urea m/1 4m	Unchanged.		Unchanged.	Unchanged.		Strong sol. stim. force. Otherwise indifferent.
HCl m/64 m/32	Rise.			Rise.	Rise.	1 min.	HCl m/64 m/32	Less.		Less.			Weak stim. briefly strong sol. depres.
NH_4Cl m/64 m8				m/8 Rise.	m/8 Rise.		NH_4Cl m/64 m8	Less. m⅝	Less m⅝			m⅝ less.	m⅝ depress., m/8 stim. expir. and blood press.
Na_2SO_4 m/2 m/1	Rise.			Rise.	Rise.		Na_2SO_4 m/2 m/1						Stim. force and press.
$BaCl_2$ m/64 m/4	Rise.			Rise.	Rise.		$BaCl_2$ m/64 m/4						m/4 toxic, weak sol. stim. force. Pres. prolonged diastole,
Distilled water.	Brief rise.				Brief rise.		Distilled water.	Less.		Less.			Brief stim. for blood press. and cardiac force.
NaH_2PO_4 m/64 m/8	Rise.	Rise.	Rise.	Rise.			NaH_2PO_4 m/64 m/8						Weak sol. stim. rate and force, prolong inspir. & diastole.

TABLE XVI. Toxic and Antitoxic Solutions.

Toxic.	Antitoxic.	Curves.
2m NaCl.	$CaCl_2$ m/32	3
m⅝ KCl.	m⅝ NaCl	11
m⅝ KCl.	$CaCl_2$ m/32	12
m⅝ KCl.	$CaCl_2$ m/4	13
m/1 $NMgSO_4$	$CaCl_2$ m/8	14
NaH_2PO_4 m/4	Na_2HPO_4, or $CaCl_2$ m/16	
m/1 Na_2SO_4	$CaCl_2$ m/16	
$BaCl_2$ m/4	$CaCl_2$ m/8	
$BaCl_2$ m/4	NaOH m/8	
NaOH m/16	HCl m/100	

The following is a *résumé* of the conclusions drawn from the different experiments:

M⅝ NaCl increases the force of cardiac and respiratory rhythm and blood pressure, but is indifferent to the rate during the first five minutes. Weaker solutions are neutral, and a stronger, m/1, solution is rather depressing except to heart force and blood pressure, while 2m is generally depressing, prolonging systolic and inspiratory phases.

The different strengths of KCl solutions proved depressing to the activities under consideration. Diastole and inspiratory changes are prolonged and the toxic effect of an m⅝ solution is counteracted by CaCl m/32 or NaCl m⅝.

$CaCl_2$ solutions are indifferent or depressing to the rate of both cardiac and respiratory activities, but stimulating to the force and slightly so to the blood pressure. M⅝ solutions prolong systolic and inspiratory phases.

Solutions of $MgSO_4$ are depressing to the respiratory mechanism and cardiac rate, but at first stimulate heart force and blood pressure. Diastole and expiratory phases are prolonged and the toxic effects are neutralized by m/8 $CaCl_2$ solutions.

Na_2CO_3 solutions stimulate heart force and blood pressure and are indifferent to the heart rate and the respiratory mechanism. Their stimulating effect upon the force of cardiac activity is enhanced when the solution is combined with urea, and like the latter exerts a similar influence upon respiration and heart action.

Na_2HPO_4 solutions stimulate as a rule only the force of heart action. The blood pressure, heart rate, as well as respiratory activities, are generally decreased or unaltered.

Solutions of NaOH proved more stimulating to cardiac force and blood pressure than any of the other solutions that were employed. They were depressing to cardiac rate and respiratory activity, except in strong solutions they increased the rate of respiration. They affect the center that controls the force of the heart-beat oppositely from what they do the center which governs the respiratory force. Like other alkaline solutions, they may exert their influence by favoring oxidation.

Urea solutions, except the strongest, are quite indifferent to the functions under consideration. A 4m solution increases the force of both the cardiac and respiratory activities; possibly through the OH ions that are set free when dissociation occurs.

Weak HCl solutions produce initial stimulations for a brief period in cardiac and respiratory force and blood pressure, but depress the rate, and a stronger, m/8, solution is toxic for cardiac but less so for respiratory activity.

Weak solutions of NH_4Cl are indifferent. An m/8 has a slight augmenting effect on blood pressure and the expiratory phase, while an m5/8 solution depresses blood pressure and cardiac rhythm, but heightens the force of the respiratory mechanism for a short time.

Following the injection of strong Na_2SO_4 solutions the force of respiration and heart action and height of blood pressure is increased, while the rate is unchanged. The addition of a weak solution of $CaCl_2$ is favorable.

The effect of a weak solution of $BaCl_2$ is increased force of cardiac and respiratory rhythm and a rise of blood pressure. Diastolic and expiratory phases are prolonged. The solutions are more toxic than other salts of the same concentration, and the toxicity is overcome by $CaCl_2$.

Injections of distilled water produce transient stimulating effects in the force of cardiac contractions and blood pressure, and depress the rate.

Weak solutions of NaH_2PO_4 accelerate the rate and force of heart and respiratory action. Diastole and inspiration are prolonged and toxic solutions are neutralized by Na_2HPO_4.

A consideration of the results tabulated in the foregoing

pages discloses the fact that increased force of cardiac activity is usually accompanied by increased force of respiratory action and blood pressure. But NH_4CL m/8, urea, and Na_2HPO_4 are exceptions. NH_4Cl increases blood pressure without increasing cardiac force. Urea produced increased force of respiratory and cardiac activity without raising blood pressure, and Na_2HPO_4 m/8 increases force of cardiac but decreases force of respiratory action. Moreover, most of the salt solutions of a definite concentration that augmented the force of cardiac also increased the force of the respiratory rhythm and proved either indifferent or depressing in their influence upon the rate of both of these activities.

The exceptions are $MgSO_4$ m/8, which stimulates force of cardiac but not that of respiratory activities and is depressing to rate, and NaOH m/8, that stimulates cardiac force and rate but not the respiratory rhythm.

The toxic effect of many solutions at certain concentrations was counteracted by definite strengths of other salts. Of these antagonistic solutions, $CaCl_2$ m/32 or m/8 proved most extensively favorable. It was interesting to learn that certain concentrations of some salt solutions prolong the cardiac systole and the inspiratory phases, while other solutions favor diastolic and expiratory phases. M/2 NaCl and also m⅝ $CaCl_2$ prolong systole and inspiration, while KCl m/8, NaH_2PO_4 m/8 prolong inspiratory activity and diastole. Moreover, strong solutions of $MgSO_4$, NH_4Cl and $BaCl_2$ prolong diastole and expiratory activity.

The salts that were especially depressing upon the cardiac and respiratory phases were KCl and $MgSO_4$. There are certain optimum per cents of salts and acid solutions, below or weaker than which the effect is stimulating or initiates temporarily increased activity, and above or greater concentration than which the solution inhibits or decreases activity or proves toxic. Moreover, increased blood pressure, as a rule, is accompanied by a decrease in rate of cardiac and respiratory activity.